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OLSON, ERIC	
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NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/767,019	WRIGHT, GEORGE E.	
	Examiner	Art Unit	
	ERIC S. OLSON	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,7,8,10-19,32-34 and 36-50* is/are pending in the application.

4a) Of the above claim(s) *41 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,7,8,10-19,32-34,36-40 and 43-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/17/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 17, 2009 has been entered.

Detailed Action

This office action is a response to applicant's communication submitted February 17, 2009 wherein claims 1, 32, and 45 are amended, claims 4, 6, 9, and 35 are cancelled, and new claims 47-50 are introduced. This application claims benefit of provisional application 60/443519, filed January 29, 2003.

Claims 1-3, 5, 7, 8, 10-19, 32-34, and 36-50 are pending in this application.

Claims 1-3, 5, 7, 8, 10-19, 32-34, 36-40, and 43-50 as amended are examined on the merits herein.

The following new grounds of rejection are introduced:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 7, 8, 10, 14, 16-18, 32-34, 36, 43, 45, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wright et. al. (U.S. Patent No. 5,646,155; Of record)in view of Gilbert et. al. (Reference included with PTO-892).

Wright discloses a pharmaceutical composition for the treatment of herpes virus infection comprising an inhibitor of Herpes simplex virus thymidine kinase wherein one of the compounds may be a 6-oxo (guanine) compound with or without substitution at the 9- position (col. 7, line 66 - col. 8, line 5). Wright also teaches that the compound(s) may be combined with other direct antiviral
drugs (col. 9, lines 59-62) and may be administered in a variety of formulations, for example parenteral or oral formulations, and formulations containing sterile water or saline, and polymers such as biodegradable lactide polymer. (col. 9, lines 16-57)

Wright does not expressly disclose any particular combination of an inhibitor of Herpes simplex virus thymidine kinase and another antiherpes substance that is a nucleoside or pyrophosphate analog according o the instant claims or a kit comprising said combination.

Gilbert et al. discloses therapeutic agents useful for treating herpesvirus infection, for example the acyclic nucleoside phosphonate derivative cidofavir and the pyrophosphate analog foscarnet. (p. 88 right column last paragraph)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising a combination of an inhibitor of Herpes Simplex virus thymidine kinase and an antiherpes substance comprising one or

more of a (1) a pre-phosphorylated or phosphonate nucleoside analog such as cidofavir, or a pyrophosphate analog such as foscarnet since Wright et. al. discloses pharmaceutical compositions comprising a herpes simplex virus thymidine kinase inhibitor and suggests the combination with other direct antiviral drugs.

One of ordinary skill in the art would have been motivated to make a combination of an inhibitor of herpes simplex thymidine kinase and another antiherpes agent since Wright suggests combination of a oxo-guanine thymine kinase inhibitor with other antiherpes agents.

Therefore, one of ordinary skill in the art would have reasonably expected that the combination of an inhibitor of herpes simplex thymidine kinase and another antiherpes agent would have resulted in substantially similar or beneficial effects in the treatment of herpes infection.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. See In re Kerkhoven, 205 USPQ 1069, CCPA 1980. Furthermore, one of ordinary skill in the art would have been motivated to prepare a kit comprising the same composition because the preparation of a kit comprising a pharmaceutical composition is considered well in the competence level of an ordinary skilled artisan and well within conventional skills in pharmaceutical science, involving merely routine skill in the art.

As regards the new limitation requiring that the two components be used in a dose that is less than the median therapeutically effective dose of the compound used alone, one of ordinary skill in the art would have expected an additive therapeutic effect from combining two compositions useful for treating the same condition, for example herpes. Therefore one of ordinary skill in the art would have realized that the amount of each of the two components necessary to achieve an adequate therapeutic effect is less than the median effective dose of each agent when used individually.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claims 1-3, 5, 7, 8, 11-14, 15-18, 32-34, 37-40, and 43-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wright et. al. (U.S. Patent No. 5,646,155; Of record) in view of Hostetler. (US patent 5879700, cited in PTO-892).

Wright discloses a pharmaceutical composition for the treatment of herpes virus infection comprising an inhibitor of Herpes simplex virus thymidine kinase wherein one of the compounds may be a 6-oxo (guanine) compound with or without substitution at the 9- position (col. 7, line 66 - col. 8, line 5). Wright also teaches that the compound(s) may be combined with other direct antiviral drugs (col. 9, lines 59-62) and may be administered in a variety of formulations, for example topical formulations, and formulations containing sterile water or saline, and polymers such as biodegradable lactide polymer. (col. 9, lines 16-57)

Wright does not expressly disclose any particular combination of an inhibitor of Herpes simplex virus thymidine kinase and another antiherpes substance that is a nucleoside or pyrophosphate analog according o the instant claims or a kit comprising said combination.

Hostetler discloses topical drugs for treating herpes including acyclovir monophosphate (column 3 lines 35-66) and monophosphates, diphosphates, and other phosphate esters of other nucleoside analogs including gancyclovir. (column 5 line 15 - column 6 line 38) These phosphates are reasonably considered to be phosphate esters of acyclovir and ganciclovir. These compounds are applied as topical formulations, for example aqueous solutions, water-in-oil emulsions, and aqueous creams, or a dry powder formulation, which would be a formulation containing particles. (column 9 lines 44-60)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising a combination of an inhibitor of Herpes Simplex virus thymidine kinase and an antiherpes substance comprising acyclovir monophosphate or ganciclovir monophosphate since Wright et. al. discloses pharmaceutical compositions comprising a herpes simplex virus thymidine kinase inhibitor and suggests the combination with other direct antiviral drugs.

One of ordinary skill in the art would have been motivated to make a combination of an inhibitor of herpes simplex thymidine kinase and another antiherpes agent since Wright suggests combination of a oxo-guanine thymine kinase inhibitor with other

antiherpes agents, and Hostetler discloses other active agents that can be administered topically.

Therefore, one of ordinary skill in the art would have reasonably expected that the combination of an inhibitor of herpes simplex thymidine kinase and another antiherpes agent would have resulted in substantially similar or beneficial effects in the treatment of herpes infection.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. See In re Kerkhoven, 205 USPQ 1069, CCPA 1980. Furthermore, one of ordinary skill in the art would have been motivated to prepare a kit comprising the same composition because the preparation of a kit comprising a pharmaceutical composition is considered well in the competence level of an ordinary skilled artisan and well within conventional skills in pharmaceutical science, involving merely routine skill in the art.

As regards the new limitation requiring that the two components be used in a dose that is less than the median therapeutically effective dose of the compound used alone, one of ordinary skill in the art would have expected an additive therapeutic effect from combining two compositions useful for treating the same condition, for example herpes. Therefore one of ordinary skill in the art would have realized that the amount of each of the two components necessary to achieve an adequate therapeutic effect is less than the median effective dose of each agent when used individually.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

The following rejections of record in the previous action are maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, 7, 8, 10-19, 32-34, and 36-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation, "analog" in these claims render claims herein indefinite. The recitations, "analog" of the compounds are not clearly defined in the specification. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to "analog" of compounds herein. One of ordinary skill in the art would clearly recognize that analog of a nucleoside or a pyrophosphate or phosphonate nucleoside analog would read on any those compounds having any widely varying groups that possibly substitute the compounds.

Any significant structural variation to a compound would be reasonably expected to alter its properties; e.g., physical, chemical, physiological effects and functions. Thus, it is unclear and indefinite as to the "analog" of compounds herein encompassed thereby.

Response to Argument: Applicant's arguments, submitted February 17, 2009, with respect to the above ground of rejection, has been fully considered and not found to be persuasive to remove the rejection. Applicant argues that the metes and bounds of nucleoside analogs that are "an antiherpes substance that inhibits viral DNA replication" are well-understood by those of ordinary skill in the art. However, while there are certainly a lot of nucleoside analogs and pyrophosphate analogs that are known in the art, claims are given their broadest reasonable interpretation, which includes a vast number of marginal structures that may or may not be nucleoside or pyrophosphate analogs. By its very nature, a term like "analog" is open to interpretation and those skilled in the art will disagree about where to draw the line between compounds that are and are not analogs. Therefore this term cannot be definite, and the rejection is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 7, 8, 14-19, 32, 34, 39, 40 and 50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for one of a composition comprising 2- phenylamino-6-oxo-9-(4-hydroxybutyl)purine with an antiherpes substance such as foscarnet, acyclovir, ganciclovir, or cidoforvir, does not reasonably provide enablement for the use of a combination of an inhibitor of Herpes simplex virus thymidine kinase with any antiherpes substance comprising one or more of a pre-

phosphorylated or phosphonate nucleoside analog, a pyrophosphate analog and a nucleoside analog or esters of said drugs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention:

The claimed invention is a therapeutic method for treating a herpes simplex viral infection using combination therapy.

The relative skill of those in the art:

The relative skill of those in the art is high, with a typical practitioner having obtained a PhD, M.D. or equivalent advanced degree.

The breadth of the claims:

The current claims are deemed very broad since they include the combination of any compound that is an inhibitor of Herpes simplex virus thymidine kinase and any one of the large classes of compounds encompassed by the descriptions pre-

phosphorylated or phosphonate nucleoside analog, or pyrophosphate analog or nucleoside analog or any combination thereof or an ester salt or solvate thereof. The compound to be combined includes all known drugs used for the treatment of said diseases as well as the ones to be developed in the future.

The amount of direction or guidance presented and the presence or absence of working examples:

There are only three working examples of combination therapy provided. Table 2 (Page 13, line 35 to page 14, line 8) describes the efficacy of a combination of HBPG with foscarnet. Each of the examples discloses a combination of HBPG with one of the three well known antiherpes agents. The broad claims herein are directed to a combination of a broad class of compounds with any one or more of the compounds selected from another three broad classes of compounds. As such, the disclosure of the working examples is not commensurate with the claims herein. For example, no representative from the class of pyrophosphate analog is shown as a working example in combination with an inhibitor of Herpes simplex virus thymidine kinase.

The predictability or lack thereof in the art and the quantity of experimentation necessary:

Combination therapy is known in the art to have various effects, and when physicians use several drugs in combination, they face the problem of knowing whether a specific combination in a given patient has the potential to result in a drug-drug interaction, and if so, how to take advantage of the interaction if it leads to improvement in therapy or how to avoid the consequences on an interaction if they are adverse. A

potential drug interaction refers to the possibility that one drug may alter the intensity of the pharmacological effects of another drug if given concurrently. The net result may be enhanced or diminished effects of one or both of the drugs, or the appearance of new effects, which is not seen with either drug alone. The frequency of significant beneficial or adverse effects is unknown. The interaction between the drugs may be pharmacokinetic, i.e. alteration of the absorption, distribution, or elimination of one drug by another, or may be pharmacodynamic, i.e. interactions between agonists and antagonists at drug receptors. The most important drug-drug interactions occur with drugs that have serious toxicity and low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences. Additionally, drug-drug interactions can be clinically important if the disease being controlled with the drug is serious or potentially fatal if left under treated. Drugs are known to interact at any point during their absorption, distribution, metabolism, or excretion; the result being an increase or decrease in concentration of the drug at the site of action. As individuals vary in their rates of disposition of an given drug, the magnitude of an interaction that alters pharmacokinetic parameters is not always predictable, but can be very significant. See Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 10 th Edition, McGraw-Hill Medical Publishing Division, 2001, pages 54-56. (Of record) Thus, the teachings of the book clearly support that the instant claimed invention, administering a combination of an inhibitor of Herpes Simplex virus thymidine kinase and an antiherpes substance comprising one or more of a pre-phosphorylated or phosphonate nucleoside analog, a pyrophosphate analog and a nucleoside analog.

The usefulness of HBPG with one of the three compounds does not mean that any compound with activity as inhibitor of Herpes simplex virus thymidine kinase will be useful for combination therapy with one or more of a compound selected from the classes of compounds considered as a pre-phosphorylated or phosphonate nucleoside analog, a pyrophosphate analog and a nucleoside analog.

In particular, one skilled in the art would need to know whether the regular administration of the combination in the claimed form over the long term would adversely affect the health of the subject.

In order to answer these questions, in the absence of any existing data, one skilled in the art, will have to undertake laboratory and clinical studies involving different combinations of one of the broad class of compounds with activity against Herpes simplex virus thymidine kinase and one of any of a large series of compounds selected from pre-phosphorylated or phosphonate nucleoside analogs, a pyrophosphate analogs and nucleoside analogs. Accomplishing such a task for the treatment of herpes infection will require an undue amount of experimentation for the practice of full range of the claimed invention.

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, especially the breadth of the claims, the unpredictability of the art, and the lack of guidance or working

examples, Applicants fail to provide information sufficient to practice the claimed invention for the combination therapy claimed herein absent undue experimentation.

Response to Argument: Applicant's arguments, submitted February 17, 2009, with respect to the above ground of rejection, has been fully considered and not found to be persuasive to remove the rejection. Applicant argues that one skilled in the art could have readily obtained inhibitors of thymidine kinase and substances that inhibit DNA replication as covered by the claims. However, while one skilled in the art could have made and used the specific purine inhibitors of thymidine kinases used in the claims, nucleoside analogs and pyrophosphate analogs cover a broad range of incompletely defined or characterized compounds. Furthermore, Applicant argues that antiherpes substances that inhibit viral DNA replication are a class of compounds readily known to a person of ordinary skill in the art. Actually, they are not. While some such inhibitors, for example acyclovir, are known, the range of substances that can inhibit DNA replication is much wider than the narrow scope of related compounds that are known in the art. The work of discovering and characterizing the full scope of these compounds has not been done, either by the Applicant, or by anyone else in the art. The experimentation required to render these compounds known and usable would be undue and unpredictable. Therefore they are not enabled and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 7, 8, 10, 14, 16-18, 32-34, 36, 43, 45, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wright et. al. (U.S. Patent No. 5,646,155; Of record)in view of Naesens et. al. (Herpes, 8(1), 2001 ; Of record).

Wright discloses a pharmaceutical composition for the treatment of herpes virus infection comprising an inhibitor of Herpes simplex virus thymidine kinase wherein one of the compounds may be a 6-oxo (guanine) compound (col. 7, line 66 - col. 8, line 5). Wright also teaches that the compound(s) may be combined with other direct antiviral drugs (col. 9, lines 59-62) and may be administered in a variety of formulations (col. 9, lines 16-57).

Wright does not expressly disclose any particular combination of an inhibitor of Herpes simplex virus thymidine kinase and another antiherpes substance or a kit comprising said combination.

Naesens discloses a series of antiherpes substances including acyclovir, ganciclovir, cidofavir, foscarnet and brividin. (Abstract; Pages 13-15). Naesens discloses Foscarnet and cidofovir as antiherpes agents independent of thymidine kinase.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising a combination of an inhibitor of Herpes Simplex virus thymidine kinase and an antiherpes substance comprising one or more of a (1) a pre-phosphorylated or phosphonate nucleoside analog, a pyrophosphate analog and a nucleoside analog since Wright et. al. discloses pharmaceutical compositions comprising a herpes simplex virus thymidine kinase inhibitor and suggests the combination with other direct antiviral drugs.

One of ordinary skill in the art would have been motivated to make a combination of an inhibitor of herpes simplex thymidine kinase and another antiherpes agent since Wright suggests combination of a oxo-guanine thymine kinase inhibitor with other antiherpes agents.

Therefore, one of ordinary skill in the art would have reasonably expected that the combination of an inhibitor of herpes simplex thymidine kinase and another antiherpes agent would have resulted in substantially similar or beneficial effects in the treatment of herpes infection.

It has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form a third composition that is to be used for very same purpose. The idea of combining them flows logically from their having been individually taught in prior art. See In re Kerkhoven, 205 USPQ 1069, CCPA 1980. Furthermore, one of ordinary skill in the art would have been motivated to prepare a kit comprising the same composition because the preparation of a kit comprising a pharmaceutical composition is considered well in

the competence level of an ordinary skilled artisan and well within conventional skills in pharmaceutical science, involving merely routine skill in the art.

As regards the new limitation requiring that the two components be used in a dose that is less than the median therapeutically effective dose of the compound used alone, one of ordinary skill in the art would have expected an additive therapeutic effect from combining two compositions useful for treating the same condition, for example herpes. Therefore one of ordinary skill in the art would have realized that the amount of each of the two components necessary to achieve an adequate therapeutic effect is less than the median effective dose of each agent when used individually.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Response to Argument: Applicant's arguments, submitted February 17, 2009, with respect to the above ground of rejection, has been fully considered and not found to be persuasive to remove the rejection. Applicant argues that the prior art teaches that thymidine kinase inhibitors antagonize the activity of other antiherpes drugs, therefore discouraging one of ordinary skill in the art from combining these two classes of drugs at concentrations less than the median therapeutic dose. However both of the cited references Ashton et al. and Klein et al. disclose that the nucleoside analogs acyclovir and ganciclovir are dependent on phosphorylation by thymidine kinase to be metabolized into their active form, resulting in their being antagonized by drugs that inhibit thymidine kinase. One of ordinary skill in the art would have realized that this effect is limited to those drugs that depend on thymidine kinase to be activated *in vivo*.

Therefore one of ordinary skill in the art would expect drugs that already contain a phosphate group and which need no activation *in vivo*, for example foscarnet and cidofovir, not to be antagonized by thymidine kinase inhibitors. Thus one of ordinary skill in the art would expect these drugs to produce an additive effect when co-administered with other drugs such as the thymidine kinase inhibitors described by Wright, and to therefore produce a therapeutic effect at less than the does required to produce a therapeutic effect alone.

Thus the rejection is deemed proper and maintained.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. OLSON whose telephone number is (571)272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/
Examiner, Art Unit 1623
4/29/2009